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Catalytic Oxyalkylation of Alkenes with Alkanes and Molecular Oxygen via a Radical Process Using *N*-Hydroxyphthalimide

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A novel catalytic method for the radical addition of alkanes and molecular oxygen to electron-deficient alkenes was achieved by the use of *N*-hydroxyphthalimide (NHPI) combined with a Co species as the catalyst. This reaction is referred to as oxyalkylation of alkenes with alkanes and O_2. For instance, the reaction of 1,3-dimethyladamantane with methyl acrylate under molecular oxygen in the presence of catalytic amounts of NHPI and $Co(acac)_3$ at 70 °C for 16 h gave oxyalkylated products in 91% yield. Other alkenes such as fumarate and acrylonitrile also serve as good acceptors of alkyl radicals and O_2 to afford the corresponding adducts in high yields. The generality of the present reaction was examined between various alkanes and alkenes under dioxygen. The behavior of Co ions during the reaction course was discussed. The present reaction involves (i) an alkyl radical generation via hydrogen abstraction of alkane by phthalimide *N*-oxyl generated in situ from NHPI and O_2 assisted by Co(II), (ii) the addition of the resulting alkyl radical to an electron-deficient alkene to form an adduct radical, (iii) trapping of the adduct radical by O_2 yielding a hydroperoxide, and (iv) the decomposition of the hydroperoxide by Co ions to form an adduct in which a hydroxy or a carbonyl function is incorporated.

Introduction

Radical reactions have become a very useful synthetic tool because of the many advantages over ionic reactions, and much attention has been paid to the development of efficient carbon–carbon bond-forming reactions.[1] Various methods have been developed for the generation of alkyl radicals; e.g., the reaction of alkyl halides with tributyltin hydride[2] or tris(trimethylsilyl)silane,[3] the thermal decomposition of Barton esters,[4] the photolysis of alkylcobalt compounds,[5] the reaction of triethylborane under dioxygen,[6] etc. However, the generation of alkyl radicals through the direct C–H bond homolysis of alkanes has remained elusive. Current methods for the alkyl radical generation by the homolysis of alkanes are generally based on peroxide- and photoinitiated techniques[1,7] or redox systems using metal ions.[8] Therefore, we believe that the catalytic generation of alkyl radicals from alkanes and its use in carbon–carbon bond-forming reactions are a worthwhile endeavor in free-radical chemistry, since work on such methodology has so far been limited.[9]

Recently, we have reported a novel catalytic aerobic oxidation of alkanes employing *N*-hydroxyphthalimide (NHPI) as the catalyst under mild conditions, and proposed that phthalimide *N*-oxyl (PINO) generated from NHPI and dioxygen is a key radical species. The PINO formed abstracts a hydrogen atom from alkanes to form alkyl radicals that are readily captured by O_2 to give oxygenated compounds such as alcohols, ketones, and carboxylic acids.[10] In continuation of this work, we have been interested in the addition of alkyl radicals generated from alkanes to alkenes leading to the formation of a new carbon–carbon bond. Furthermore, since the generation of PINO from NHPI is carried out under dioxygen atmosphere, we envisioned the concomitant introduction of alkyl and oxygen functions to the alkenes. This new type of reaction may be regarded as a catalytic oxyalkylation of alkenes with alkanes and dioxygen, which so far has not been fully successful (Scheme 1).

In this paper, we wish to report the first catalytic oxyalkylation of alkenes with alkanes and molecular oxygen using NHPI as the catalyst.[11]

(1) (a) Giese, B. In *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*; Pergamon: Oxford, 1986. (b) Curran, D. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Semmelhack, M. F., Eds.; Pergamon: Oxford, 1991; Vol. 4, p 715. (c) Motherwell, W. B.; Crich, D. In *Free-Radical Reactions in Organic Synthesis*; Academic Press: London, 1992. (d) Fossey, J.; Lefort, D.; Sorba, J. In *Free Radicals in Organic Synthesis*; Wiley: Chichester, 1995. (e) Parsons, A. F. In *An Introduction to Free Radical Chemistry*; Blackwell Science: Oxford, 2000. (f) Chatgilialoglu, C.; Renaud, P. In *General Aspects of the Chemistry of Radicals*; Alfassi, Z. B., Eds.; Wiley: Chichester, 1999; pp 501–538.

(2) Reviews: (a) Neumann, W. P. *Synthesis* **1987**, 665. (b) Curran, D. P. *Synthesis* **1988**, 417. (c) Davies, A. G. In *Organotin Chemistry*; Wiley-VCH: Weinheim, 1997. (d) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 753.

(3) (a) Chatgilialoglu, C. *Acc. Chem. Res.* **1992**, *25*, 7019. (b) Dowd, P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091.

(4) (a) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901. (b) Crich, D. *Aldrichim. Acta* **1986**, *20*, 35. (c) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541.

(5) (a) Pattenden, G. *Chem. Soc. Rev.* **1988**, *17*, 361. (b) Branchaud, B. P.; Meier, M. S.; Choi, Y. *Tetrahedron Lett.* **1988**, *29*, 167.

(6) (a) Brown, H. C.; Negishi, E. *J. Am. Chem. Soc.* **1971**, *93*, 3777. (b) Brown, H. C.; Midland, M. M. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 692 and references therein.

(7) (a) Hill, C. L. *Synlett* **1995**, 127. (b) Tabushi, I.; Fukunishi, K. *J. Org. Chem.* **1974**, *39*, 3748. (c) Tabushi, I.; Kojo, S.; Fukunishi, K. *J. Org. Chem.* **1978**, *43*, 2370.

(8) Caronna, T.; Citterio, A.; Crolla, T.; Minisci, F. *Tetrahedron Lett.* **1976**, 1731. (b) Caronna, T.; Citterio, A.; Crolla, T.; Minisci, F. *J. Chem. Soc., Perkin Trans. 1* **1977**, 865.

(9) (a) Zheng, Z.; Hill, C. L. *Chem. Commun.* **1998**, 2467. (b) Hill, C. L. *Synlett* **1995**, 127. (c) Minisci, F. *Synthesis* **1973**, 1.

(10) (a) Ishii, Y.; Iwahama, T.; Sakaguchi, S.; Nakayama, K.; Nishiyama, Y. *J. Org. Chem.* **1996**, *61*, 4520. (b) Sakaguchi, S.; Kato, S.; Iwahama, T.; Ishii, Y. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1237. (c) Iwahama, T.; Sakaguchi, S.; Nishiyama, Y.; Ishii, Y. *Tetrahedron Lett.* **1995**, *36*, 6923. (d) Yoshino, Y.; Hayashi, Y.; Iwahama, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **1997**, *62*, 6810.

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Scheme 1. Our Strategy for the Present Reaction

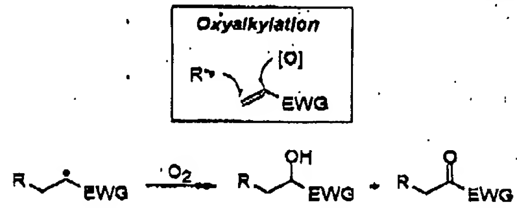
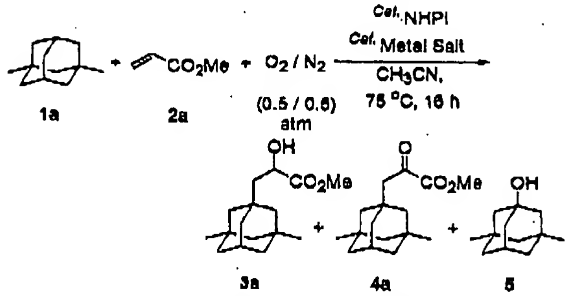


Table 1. Reaction of 1,3-Dimethyladamantane (1a) with Methyl Acrylate (2a) under Dioxygen[a]



run	metal salt	convn/%	yield[b]/% (ratio of 3a/4a)
1	Co(acac)$_2$	60	48 (71/29)
2[c]	Co(acac)$_3$	20	>5 (60/40)
3	Co(OAc)$_2$	81	46 (70/30)
4	Co(acac)$_3$	93	91 (67/33)
5[c]	Co(acac)$_3$	25	>5 (60/40)
6	Mn(acac)$_2$	92	62 (56/44)
7	Mn(acac)$_3$	85	55 (58/42)
8[d]	VO(acac)$_2$	92	38 (23/77)
9[d]	Cu(acac)$_2$	81	37 (19/81)
10[d]	Fe(acac)$_3$	76	18 (33/67)

[a] A mixture of **1a** (15 mmol), **2a** (3 mmol), NHPI (0.6 mmol), metal salt (0.03 mmol), and CH_3CN (8 mL) was stirred under O_2/N_2 (0.5/0.5 atm) at 75 °C for 16 h. In all runs, a small amount of adamantanol **5** was detected. [b] Based on **2a** reacted. [c] Without NHPI. [d] Polymers of **2a** were formed as major products.

Results

At the first instance, the oxyalkylation of methyl acrylate (**2a**) with 1,3-dimethyladamantane (**1a**) under dioxygen catalyzed by NHPI combined with a Co species was chosen as a model reaction, and several control experiments were carried out to confirm the optimum conditions.

Previously, we showed that a Co(III)–dioxygen complex formed from Co(II) and O_2 accelerates the formation of PINO from NHPI under mild conditions.[12] Thus, the reaction of **1a** with **2a** under a mixed gas of O_2 (0.5 atm) and N_2 (0.5 atm) catalyzed by NHPI (20 mol %) in the presence of Co(acac)$_2$ (1 mol %) in CH_3CN at 75 °C for 16 h gave about a 7:3 mixture of oxyalkylated products, methyl 3-(3,3′-dimethyladamantyl)-2-hydroxy propionate (**3a**) and methyl 3-(3,3′-dimethyladamantyl)-2-oxopropionate (**4a**), in 48% yield (run 1, Table 1). Interestingly, when Co(acac)$_3$ was used in place of Co(acac)$_2$, the total yield of **3a** and **4a** was markedly improved (run 4).[13] To the best of our knowledge, this is the first successful simultaneous introduction of alkyl and oxygen functions to alkenes through a catalytic process, although the peroxides-initiated simple radical addition of **1a** to maleate and fumaronitrile is reported by Fukunishi et al.[14] The reaction of **1a** with **2a** under O_2 by the combination of NHPI with several metal ions was explored. Among the metal ions examined, Co(acac)$_3$ was found to be the best additive to form oxyalkylation products in good yields. The combined catalytic systems of NHPI with Mn(acac)$_2$ or Mn(acac)$_3$ were less efficient than the NHPI–Co(acac)$_3$ system, and the combination of the NHPI with other metal salts such as V, Fe, Cu, and Ni resulted in polymers of **2a** rather than **3a** and **4a**. The same reaction by Co(acac)$_n$ (n = 2 or 3) in the absence of NHPI was sluggish to form **3a** and **4a** in very low yields (Table 1, runs 2 and 5).

Table 2. Reaction of 1a with 2a and O$_2$ in Various Solvents[a]

run	solvent	1a/mmol	Co(acac)$_3$/mmol	convn/%	yield/% (3a/4a)
1	CH_3CN	15	0.03	93	91 (67/33)
2	AcOH	15	0.03		87 (72/28)
3	PhCN	15	0.03	48	48 (72/28)
4	CH_3CN	15	0.06	94	90 (79/21)
5	CH_3CN	15	0.015	81	73 (63/37)
6[b]	CH_3CN	15	0.03	64	54 (69/31)
7	CH_3CN	9	0.03	78	60 (67/33)
8[c]	CH_3CN	15	0.03	54	38 (68/32)

[a] A mixture of **1a**, **2a** (3 mmol), NHPI (0.6 mmol), Co(acac)$_3$ and CH_3CN (8 mL) was stirred under O_2/N_2 (0.5/0.5 atm) at 75 °C for 16 h. [b] NHPI (0.3 mmol) was used. [c] Reaction was carried out at 60 °C.

From a scrutiny of solvents, acetic acid and acetonitrile were found to be good solvents, but the reaction in benzonitrile took place very slowly (Table 2, runs 1–3). When alkane **1a** was reduced from 5 to 3 equiv with respect to **2a**, the conversion was slightly lowered to give **3a** and **4a** in 60% yield (Table 2, run 7). When the NHPI used was halved, the yield of the adducts decreased to 54%. To complete the reaction in higher conversion, the reaction must be carried out at over 60 °C (Table 2, run 8). The concentration of the Co(acac)$_3$ to the NHPI had no effect on the yield of **3a** and **4a** (Table 2, runs 1, 4, and 5). The formation of **4a** may be attributed to the further oxidation of the **3a** as shown in Scheme 2.

Inspection of Figure 1 indicates that the oxygen concentration is a dominant factor in the regulation of the present oxyalkylation. The reaction under low-oxygen concentration (N_2/O_2 = 0.8/0.2 atm) resulted in **3a** and **4a** in low yield (32%), although the conversion of **2a** was high. This result is believed to be due to the fact that the addition of dioxygen to the radical species **II** leading to the **3a** and **4a** competes with the reaction of **II** with **2a** leading to telomers of **2a**, as discussed later.[15] In fact, under low oxygen concentration, products having higher molecular weight, which are considered to be telomers of the **2a** involving the adamantyl moiety, were identified by GC–MS and GC.

On the basis of these results, the reaction of **1a** with various alkenes was run under selected reaction conditions

(11) We have already reported two types of catalytic radical additions to alkenes catalyzed by NHPI under dioxygen. (a) Reaction of alcohols with α,β-unsaturated esters under dioxygen leading to α-hydroxy-γ-lactones: Iwahama, T.; Sakaguchi, S.; Ishii, Y. *Chem. Commun.* 2000, 613. (b) Hydroxyacylation of alkenes with 1,3-dioxolanes and dioxygen: Hirano, K.; Iwahama, T.; Sakaguchi, S.; Ishii, Y. *Chem. Commun.* 2000, 2457.

(12) Previous ESR measurements indicated that the radical species PINO is smoothly generated from NHPI and O_2 in the presence of Co(II) species under mild conditions: Iwahama, T.; Syojyo, K.; Sakaguchi, S.; Ishii, Y. *Org. Pro. Res., & Dev.* 1998, 2, 255 and ref 10d.

(13) The present oxyalkylation resulted in a concomitant formation of oxidation products of **1a**, 1-adamantanol (**5**). In run 4 of Table 1, **5** was obtained in 7% yield.

(14) Fukunishi, K.; Tabushi, I. *Synthesis* 1988, 826.

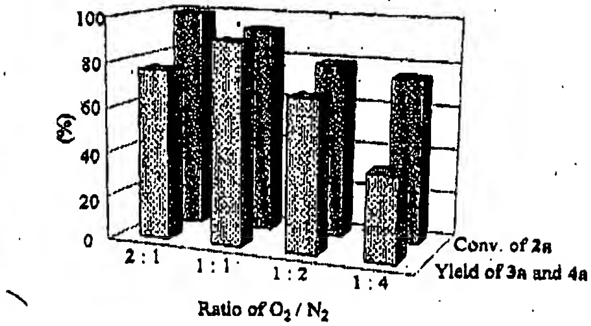
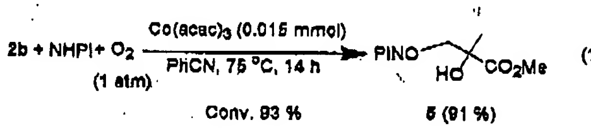


Figure 1. Reaction of **1a** with **2a** under variable O_2/N_2 ratio. Reaction conditions: **1a** (15 mmol), **2a** (3 mmol), NHPI (0.6 mmol), $Co(acac)_3$ (0.03 mmol), CH_3CN (3 mL), O_2/N_2 (total 1 atm), 75 °C, 16 h.

tions (Table 3). Methacrylate (**2b**) gave the corresponding oxyalkylated product **3b** (36%) together with an adduct **5**, which appears to be formed by the addition of the PINO radical to **2b**. An independent stoichiometric reaction of **2b** with NHPI gave **5** in 91% yield (eq 1). In



contrast, the oxyalkylation of methyl crotonate (**2c**) having a β-CH_3 group afforded adducts **3c** and **4c** in low yield (42%), probably because of the steric hindrance of the CH_3 group toward the attacking radical. Similar behavior is observed in the addition of a cyclohexyl radical to **2c**.[16] The incorporation of an electron-withdrawing substituent into the alkene decreases the SOMO–LUMO energy difference, which facilitates the addition of nucleophilic alkyl radicals to the alkenes.[16,17] Thus, methyl maleate (**2d**) and methyl fumarate (**2e**) served as good acceptors of **1a** to form the corresponding oxyalkylated products **3d** and **4d** in excellent yields. Trans isomer **2e** reacted faster than cis isomer **2d**. In general, alkyl radicals, e.g., methyl and cyclohexyl radicals, are found to add more rapidly to the trans **2e** than the cis **2d** by a factor of about 10 times.[16,18] Acrylonitrile (**2f**) and fumalonitrile (**2g**) led to alcohols **3f** and **3g**, respectively, in high selectivities. In these reactions, the resulting **3f** and **3g** bearing strong electron-withdrawing cyano group(s) resisted oxidation to ketones. Acrylamide (**2h**) was also subjected to the oxyalkylation, giving about a 1:1 mixture of alcohol **3h** and ketone **4h** in 64% yield.

Table 3. Reaction of 1a with Various Alkenes[a]

run	alkene	convn/%	products[b]	yield/% (3/4)
1[c]	CO_2Me **2b**	96	R, OH, CO_2Me **3b** + **5**	66 (55 / 45)[d]
2	CO_2Me **2c**	82	R, X, CO_2Me; X = -OH **3c**; X = =O **4c**	42 (60 / 40)
3	MeO_2C CO_2Me **2d**	86	R, X, CO_2Me, CO_2Me; X = -OH **3d**; X = =O **4d**	81 (75 / 25)
4[e]	MeO_2C CO_2Me **2e**	99	**3d** + **4d**	98 (68 / 32)
5[f,g]	CN **2f**	—	R, X, CN; X = -OH **3f**; X = =O **4f**	78 (92 / 8)
6[f,g]	NC CN **2g**	99	R, CN, OH, CN **3g**	96
7[g]	NH_2, O **2h**	96	R, X, $CONH_2$; X = -OH **3h**; X = =O **4h**	64 (53 / 47)

[a] A mixture of **1a** (27 mmol), alkene (3 mmol), NHPI (0.9 mmol), $Co(acac)_3$ (0.03 mmol), and PhCN (3 mL) was stirred under O_2/N_2 (0.5/0.5 atm) at 75 °C for 14 h. [b] R = 3,5-dimethyladamantyl. [c] AcOH (1 mL) and PhCN (7 mL) solvent, at 95 °C. [d] Ratio of **3b** and **5**. [e] **1a** (15 mmol), NHPI (0.6 mmol), 3h. [f] $Co(acac)_3$ (0.06 mmol). [g] The reaction was run in CH_3CN for 24 h. Polymers of **2h** were formed.

To survey the generality of the oxyalkylation by the present strategy, we next examined the reactions between various alkanes and methyl fumarate **2e** under dioxygen (Table 4). The reaction of adamantane (**1b**) with **2e** in a mixed solvent of chlorobenzene and PhCN proceeded with high tertiary selectivity, giving α-oxy-β-adamantylacrylate in 78% yield.[19] In a previous paper on the NHPI-catalyzed aerobic oxidation of **1b**, we showed that the hydrogen atom of the tertiary C–H bond is preferentially abstracted over the secondary one by PINO.[20] The reaction of methylcyclohexane (**1c**) with **2e** afforded the corresponding expected oxyalkylated products.

Cyclohexane (**1d**) and cyclooctane (**1e**) produced alcohols **3k** and **3l** and ketones **4k** and **4l** as well as α-hydroxy-γ-lactones **6k** and **6l**, respectively. The formation of spirolactones **6k** and **6l** can be explained by the further oxidation of the **3k** and **3l** with O_2 catalyzed by NHPI followed by the intramolecular cyclization as shown in Scheme 2. An independent reaction of **3k** in the presence of catalytic amounts of NHPI and $Co(acac)_3$

(15) Acrylates such as **2a** are known to be easily polymerized by radical initiation. Fischer et. al. have determined the accurate rate constant for the addition of $CH_2CO_2Bu^t$ radical to **1a** (k = 6 × 105 M^{-1} s^{-1}).[1b,15a] Thus, such alkenes may be difficult to be used as an acceptor in the conventional radical additions of alkyl radicals.[15b] In contrast, the present oxyalkylation seems to provide the successful addition of **1a** to acrylates, since O_2 existing in situ quickly quenches the radical intermediate to prevent the polymerization. (a) Beranek, I.; Fischer, H. In *Free Radicals in Synthesis and Biology*; Minisci, F., Ed.; Kluwer: Dordrecht, 1989; p 303. (b) Itoh, M.; Taguchi, T.; Chung, V. V.; Tokuda, M.; Suzuki, A. *J. Org. Chem.* **1972**, *37*, 2357.

(16) A β-alkyl substituent on acrylate is known to exert a powerful decelerating effect attributed to unfavorable steric interactions. The relative rate constant for the addition of a cyclohexyl radical to **2b** and **2c** is reported to be k_{2b}/k_{2c} = ca. 90; Giese, B. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 753.

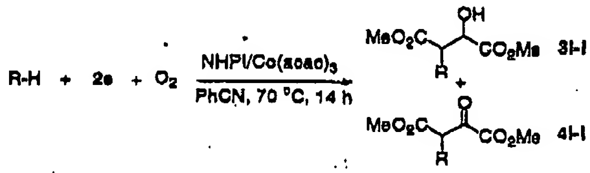
(17) Citterio, A.; Minisci, F.; Porta, O.; Sesana, G.; *J. Am. Chem. Soc.* **1977**, *99*, 7960.

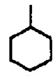
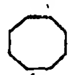
(18) Fukunishi, K.; Inoue, Y.; Kishimoto, Y.; Mashio, F. *J. Org. Chem.* **1975**, *40*, 628.

(19) Due to the low solubility of **1b** in PhCN, a mixed solvent with chlorobenzene was used. Similar to the reaction using **1a**, no secondary products could be detected.

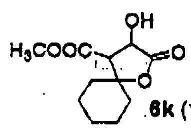
(20) The relative reactivity of tertiary hydrogen to secondary hydrogen obtained in the oxidation using NHPI catalytic system combined with Co salts is 31:1. Ishii, Y.; Kato, S.; Iwahama, T.; Sakaguchi, S. *Tetrahedron Lett.* **1996**, *37*, 4993.

Table 4. Reaction of Methyl Fumalate (2e) with Alkanes under Dioxygen[a]

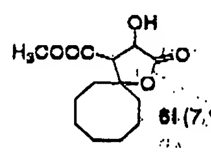


Run	R-H	Conv. / %	Yield / % (3 / 4)
1[b]	 1b	98	78 (71 / 29)
2	 1c	98	68 (71 / 29)
3[c]	 1d	99	54 (70 / 30)
4[d]	 1e	96	59 (78 / 22)

[a] Alkene (3 mmol), alkane (10 equiv.), NHPI (0.3 equiv.), Co(acac)$_3$ (0.01 equiv.) and Co(acac)$_2$ (0.005 equiv.) in PhCN (8 mL), 70°C, 14h under O_2 / N_2 (0.5 / 0.5 atm). [b] A mixed solvent of PhCN (13 mL) and PhCl (5 mL) was used.

c 

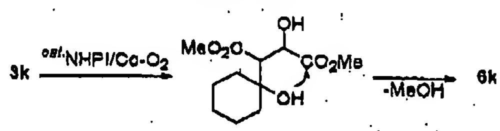
6k (16 %)

d 

6l (7 %)

under oxygen atmosphere gave the expected spiro compound **6k** in 20% yield along with **4k** (78%) (eq 2).

Scheme 2



$$\mathbf{3k} + O_2 \; (1\ \text{atm}) \xrightarrow[\text{PhCN, 75 °C, 14 h}]{\text{NHPI (0.3 mmol), Co(acac)}_3\text{ (0.03 mmol)}} \mathbf{6k}\ (20\ \%) + \mathbf{4k}\ (78\ \%) \qquad (2)$$

Discussion

To gain further insight into the role of the cobalt species in the present oxyalkylation, the reaction of **1a** with **2a** under O_2 by the NHPI/Co(acac)$_2$ system was compared with that by the NHPI/Co(acac)$_3$ system (Figure 2). In the NHPI/Co(acac)$_2$ system, the formation of **3a** and **4a** occurred very fast and was completed within 1 h, while in the NHPI/Co(acac)$_3$ system, an induction period of 0.5−1 h was observed, and then the reaction proceeded gradually to give a pair of adducts in high yield (91%). As mentioned earlier, a Co(III)−dioxygen complex derived from the Co(II) species and O_2 assists the hydrogen atom abstraction from NHPI, generating the PINO radical which abstracts the hydrogen atom from alkane to give an alkyl radical. Hence, the induction

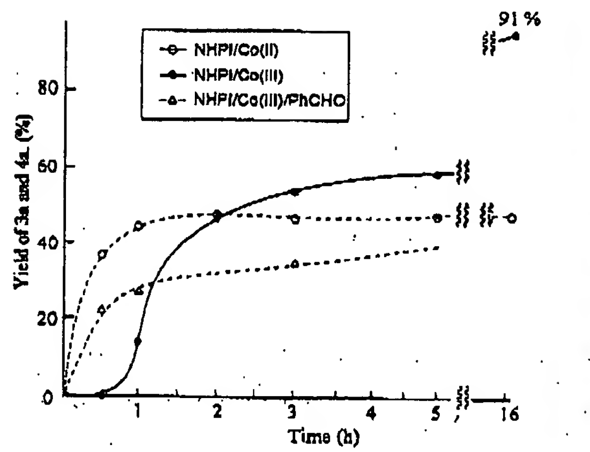


Figure 2. Time dependence curves for reaction of **1a** with **2a**. Reaction conditions: **1a** (15 mmol); **2a** (3 mmol), NHPI (0.3 mmol), Co(acac)$_3$ or Co(acac)$_2$ (0.03 mmol), CH_3CN (3 mL), O_2/N_2 (0.5/0.5 atm), 75 °C.

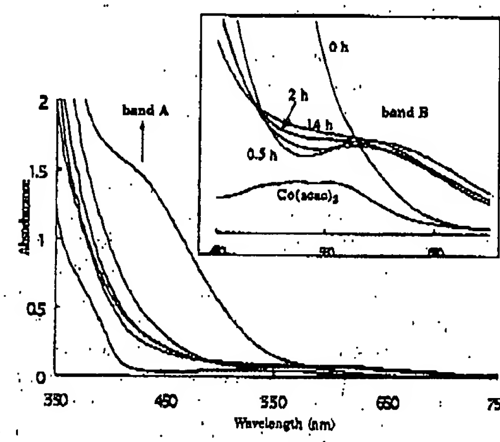


Figure 3. Time dependence of visible spectra in the reaction of **1a** with **2a** by NHPI/Co(acac)$_2$−O_2. Band at 520−570 nm increases with reaction time (0−2 h).

period observed in the NHPI/Co(acac)$_3$ system would correspond to the time needed for the generation of the Co(II) species by the reduction of Co(acac)$_3$ with **1a** and/or **2a**.[21] A Co(III) ion is known to be gradually reduced to a Co(II) ion by organic substrates such as toluene and cyclohexane via one-electron-transfer process.[22] Indeed, the addition of a small quantity of benzaldehyde to the NHPI/Co(acac)$_3$ system resulted in reduction of the induction period, because the Co(III) species is rapidly reduced with benzaldehyde to the Co(II) ion (Figure 2).

The behavior of Co ions in the reaction course of **1a** with **2a** by the NHPI/Co(acac)$_2$ and the NHPI/Co(acac)$_3$ systems was followed by measuring the visible spectra (Figures 3 and 4). In the NHPI/Co(acac)$_2$ system, the visible spectrum of the starting reaction mixture showed a band **A** (λ_{max} = ca. 420 nm) attributed to the formation of a Co(acac)$_2$−NHPI complex. After 30 min, the band **A** disappeared, and a new band **B** (λmax = 584 nm) was

(21) In the aerobic oxidation of alkylbenzenes by the NHPI/Co(II) and NHPI/Co(III), we showed that toluene is oxidized to benzoic acid by the former, but not the latter, at room temperature.[10d]

(22) Heiba, E. I.; Dessau, R. M.; Koehl, W. J. *J. Am. Chem. Soc.* **1969**, *91*, 6830. (b) Onopchenko, A.; Schulz, J. G. D. *J. Org. Chem.* **1973**, *38*, 3729.

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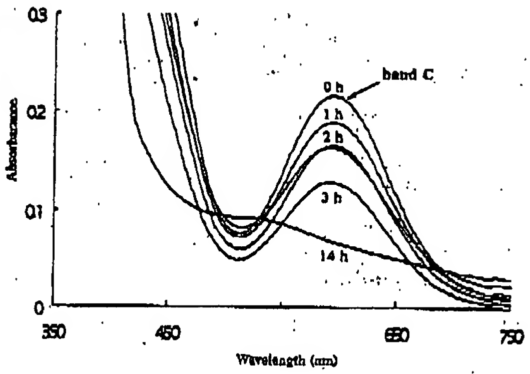


Figure 4. Time dependence of visible spectra in reaction of **1a** with **2a** by NHPI/Co(acac)$_3$–O$_2$. Band at 595 nm decreases with reaction time (0–8 h).

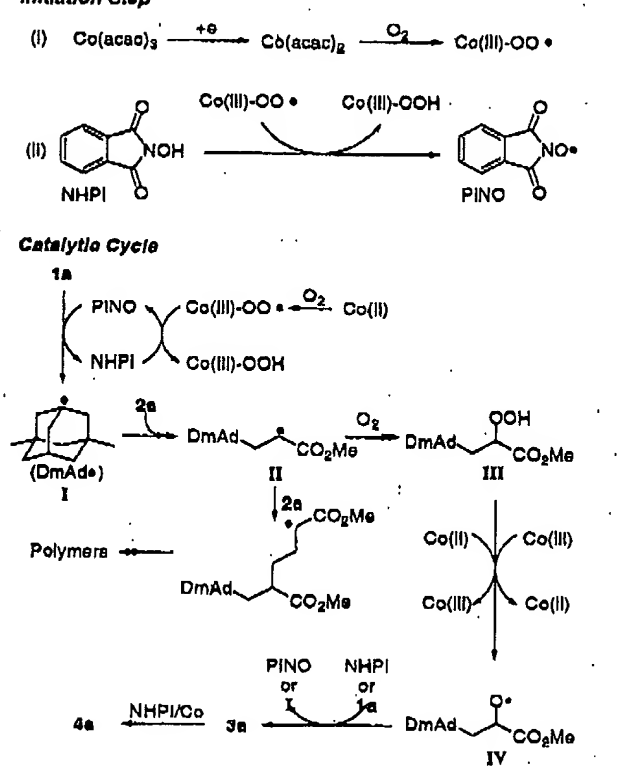
observed, which then shifted to a broad absorption band around 520–570 nm. No change in this band took place after 2 h. On the other hand, the NHPI/Co(acac)$_3$ system showed a band C at λ_{max} = 595 nm by Co(acac)$_3$. The band C gradually decreased with the reaction, and eventually changed to a band around 520–570 nm similar to that observed in the NHPI/Co(acac)$_2$.

Unfortunately, we are currently unable to explain clearly why the reaction by the NHPI/Co(acac)$_2$ system terminates at the early stage of the reaction. However, it is possible to make a proposal that seems to agree with the experimental results.

A number of divalent Co complexes, such as Co–salens, Co–porphyrins, and Co–acetylacetonates, react readily with O$_2$ to form Co–dioxygen complexes, possessing one-electron oxidation ability.[23] In the oxidation of toluene with O$_2$ at room temperature by the NHPI/Co(II) system, we have shown that the formation of Co(III)–dioxygen complexes is very important for the generation of the PINO radical, which can abstract the benzylic hydrogen atom of the toluene to form the NHPI, and the Co(III) species is reduced to a Co(II) species again in the reaction course.[10d] Hence, the concentration of Co(II) and Co(III) is balanced in the reaction. Thus, after 0.5 h in the present oxyalkylation by the NHPI/Co(acac)$_2$ system, a weak band based on a Co(III) species appeared around 580 nm. However, this band became extremely weak after 2 h and the reaction was terminated at this time. This fact shows that an unreactive cobalt complex may be formed at the early stage of the reaction by the use of the NHPI/Co(acac)$_2$ system, and it becomes difficult for this complex to form a cobalt-dioxygen complex. In contrast, in the reaction using the NHPI/Co(acac)$_3$ system, a strong band of Co(III) was continuously observed until the completion of the reaction, and finally it became a similar spectrum to that of the NHPI/Co(II) system. This observation suggests that in the reaction using the NHPI/Co(III) system, the redox system of the Co(III)/Co(II) is maintained throughout the reaction period. As mentioned above, the Co(III) species in the NHPI/Co(III) system is gradually reduced to Co(II) by organic substrates.

On the basis of these results, a plausible reaction path for the oxyalkylation of alkenes **2a** with alkane **1a** and O$_2$ using the NHPI/Co(acac)$_3$ system is shown in Scheme 3. The reaction is initiated by one-electron transfer from organic substrates to Co(acac)$_3$ to form a Co(II) species that readily reacts with O$_2$ to give a Co(III)–O$_2$ complex. The hydrogen atom abstraction from the NHPI by the action of the Co(III)–O$_2$ complex generates PINO, which then abstracts a hydrogen atom from alkane **1a** to give an alkyl radical **I**. The addition of the radical **I** to alkene **2a** produces an adduct radical **II**. Under the present conditions in which oxygen is present in the reaction system, the resulting radical **II** is rapidly trapped by O$_2$ to give a hydroperoxide **III** on which subsequent decomposition by Co ions produces an alkoxy radical **IV**. At this stage, if the oxygen concentration is low, the radical **II** adds preferentially to alkene **2a** to form telomers of **2a**. The radical **IV** abstracts the hydrogen atom from the NHPI or **1a** to yield **3a** and its oxidation product **4a**. The independent oxidation of **3a** by the NHPI combined with Co(acac)$_3$ under dioxygen (1 atm) afforded **4a** in 98% yield (eq 3).

Scheme 3. Proposed Reaction Path for the Oxyalkylation of 2a with 1a and O$_2$ in the Presence of NHPI and Co(acac)$_3$



$$\mathbf{3a} + O_2 \xrightarrow[\substack{CH_3CN,\ 75\ ^\circ C,\ 14\ h}]{\substack{NHPI\ (0.3\ mmol) \\ Co(acac)_3\ (0.03\ mmol)}} \mathbf{4a}\ (98\ \%) \qquad (3)$$
(1 atm)

In conclusion, we have developed a novel catalytic method for the oxyalkylation of alkenes with alkanes under dioxygen by the NHPI combined with a Co species. Further investigation to extend the present method and to elucidate the role of the Co species is currently in progress.

(23) (a) Wong, C. L.; Switer, J. A.; Balakrishnan, K. P.; Endicott, J. F. *J. Am. Chem. Soc.* **1980**, *102*, 5511. (b) Drago, R. S.; Cannady, J. P.; Leslie, K. A. *J. Am. Chem. Soc.* **1980**, *102*, 6014. (c) Simándi, L. I. *Catalytic Activation of Dioxygen by Metal Complexes*; Kluwer Academic: Dordrecht, 1992; pp 1–73 and references therein.

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, using $CDCl_3$ with tetramethylsilane as the internal standard. Infrared (IR) spectra were measured using NaCl or KBr pellets. Flash chromatography was performed with use of silica gel (Merck, silica gel 60, 70–230 mesh). Gas chromatography was carried out on a Shimadzu GC-17A with a flame ionization detector using a 0.22 mm × 25 m capillary column (SGE BP-5). Preparative HPLC was performed on GPC columns (JAIGEL 1H and 2H). GC–MS spectra were obtained at an ionization energy of 70 eV. Visible spectra were recorded on a Shimadzu UV-2500PC spectrophotometer. All starting materials, solvents, and catalysts were purchased from commercial sources and used without further treatment.

General Procedure for Oxyalkylation of Methyl Acrylate (2a) with 1,3-Dimethyladamantane (1a) under Dioxygen. An acetonitrile (8 mL) solution of **2a** (3 mmol), **1a** (15 mmol), NHPI (97.8 mg, 20 mol %), and Co(acac)$_3$ (10.7 mg, 1 mol %) was placed in a two-necked flask equipped with a balloon filled with O_2/N_2 (0.5:0.5 atm). The mixture was stirred at 75 °C for 16 h. After the reaction, the reaction mixture was extracted with diethyl ether. The combined extracts were dried over anhydrous $MgSO_4$. Removal of solvent under reduced pressure gave a clean liquid, which was purified by column chromatography on silica gel (*n*-hexane/AcOEt 100:1) to give **3a** and **4a**.

3-(3,5-Dimethyladamantan-1-yl)-2-hydroxypropionic acid methyl ester (3a): ^{1}H NMR ($CDCl_3$, 270 MHz) δ 4.31 (dd, J = 2.2, 9.5 Hz, 1H), 3.77 (s, 3H), 2.60 (s, 1H), 2.05 (m, 1H), 1.60 (dd, J = 2.2, 14.7 Hz, 1H), 1.10–1.43 (m, 13H), 0.86 (s, 6H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 176.8, 67.7, 52.5, 51.0, 48.9, 48.4, 43.1, 41.2, 34.1, 31.2, 30.6, 29.7; IR (NaCl) 3500, 2900, 1731, 1450, 1200, 1100 cm^{-1}. Anal. Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 72.43; H, 9.64.

3-(3,5-Dimethyladamantan-1-yl)-2-oxopropionic acid methyl ester (4a): ^{1}H NMR ($CDCl_3$, 270 MHz) δ 3.85 (s, 3H), 2.65 (s, 2H), 1.02–1.72 (m, 13H), 0.86 (s, 6H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 193.9, 178.8, 52.6, 50.5, 50.4, 48.2, 42.5, 40.5, 35.6, 31.0, 30.1, 29.8; IR (NaCl) 2897, 1731, 1455, 1276 cm^{-1}. Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.52; H, 9.02.

3-(3,5-Dimethyladamantan-1-yl)-2-hydroxy-2-methylpropionic acid methyl ester (3b): ^{1}H NMR ($CDCl_3$, 270 MHz) δ 3.76 (s, 3H), 3.08 (s, 1H), 1.36 (s, 3H), 1.01–1.99 (m, 15H), 0.76 (s, 6H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 178.9, 74.3, 52.5, 52.2, 51.0, 49.4, 49.3, 43.1, 41.1, 34.9, 31.2, 30.7, 29.8; IR (NaCl) 3533, 2895, 1731, 1454, 1257 cm^{-1}. Anal. Calcd for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 72.70; H, 10.05.

3-(3,5-Dimethyladamantan-1-yl)-2-hydroxybutanoic acid methyl ester (3c): identified as a mixture of diastereoisomers; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 4.54 (dd, J = 1.7, 5.7 Hz, 1H), 4.50 (dd, J = 2.7, 4.7 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 0.67H), 2.70 (d, J = 5.7 Hz, 1H), 2.06–2.07 (m, 1.25H), 1.10–1.56 (m, 20H), 0.82 (s, 6.67H), 0.77 (d, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 176.9, 175.7, 70.6, 67.2, 51.3, 51.1, 46.7, 46.5, 46.4, 46.3, 45.9, 45.8, 43.3, 43.2, 38.8, 38.6, 36.6, 36.5, 31.3, 31.2, 31.0, 30.8, 30.2, 30.0, 7.4, 7.2; IR (NaCl) 3523, 2898, 1731, 1453, 1230 cm^{-1}. Anal. Calcd for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 72.81; H, 9.91.

3-(3,5-Dimethyladamantan-1-yl)-2-oxobutynic acid methyl ester (4c): ^{1}H NMR ($CDCl_3$, 270 MHz) δ 3.86 (s, 3H), 3.31 (q, J = 7.09 Hz, 1H), 0.87–2.06 (m, 17H), 0.79 (s, 6H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 198.9, 162.5, 52.6, 50.3, 49.1, 45.4, 45.1, 42.3, 37.8, 30.7, 30.1, 29.0, 9.8; IR (NaCl) 2901, 1731, 1454, 1268 cm^{-1}. Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.34; H, 9.41. Found: C, 73.66; H, 9.49.

2-(3,5-Dimethyladamantan-1-yl)-3-hydroxysuccinic acid dimethyl ester (3d): identified as a mixture of diastereoisomers; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 4.59 (dd, J = 5.8, 7.2 Hz, 0.25H), 4.52 (dd, J = 2.2, 9.9 Hz, 1H), 3.78 (s, 0.67H), 3.77 (s, 3H), 3.72 (s, 3H), 3.70 (s, 0.67H), 2.54 (d, J = 2.2 Hz, 1H), 0.83 (s, 6.67H), 0.96–2.10 (m, 16.2H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 174.4, 174.3, 173.1, 172.7, 70.5, 69.3, 59.8, 57.3, 52.7, 52.3, 51.5, 51.3, 51.0, 50.7, 47.0, 46.9, 46.8, 46.7, 42.9, 42.8, 39.4, 39.2, 37.1, 37.0, 31.5, 31.4, 31.3, 31.2, 30.7, 30.6, 29.7, 29.6; IR (NaCl) 3500, 2945, 1750, 1450, 1160 cm^{-1}. Anal. Calcd for $C_{18}H_{28}O_5$: C, 66.64; H, 8.70. Found: C, 66.25; H, 8.59.

2-(3,5-Dimethyladamantan-1-yl)-3-oxosuccinic acid dimethyl ester (4d): ^{1}H NMR ($CDCl_3$, 270 MHz) δ 4.09 (s, 1H), 3.87 (s, 3H), 3.70 (s, 3H), 1.12–2.18 (m, 13H), 0.81 (s, 6H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 189.2, 168.2, 162.7, 62.3, 53.3, 52.1, 50.6, 45.9, 45.8, 42.7, 39.1, 38.4, 31.3, 30.5, 29.5; IR (NaCl) 2899, 1731, 1454, 1273, 1164 cm^{-1}. Anal. Calcd for $C_{18}H_{26}O_5$: C, 67.06; H, 8.13. Found: C, 67.13; H, 8.22.

3-(3,5-Dimethyladamantan-1-yl)-2-hydroxypropionitrile (3f): ^{1}H NMR ($CDCl_3$, 270 MHz) δ 4.59 (m, 1H), 2.48 (m, 1H), 1.65–1.77 (m, 2H), 1.06–2.08 (m, 13H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 120.9, 57.8, 50.8, 49.1, 48.7, 42.9, 40.9, 33.7, 31.2, 30.5, 29.5; IR (NaCl) 3441, 2896, 2245, 1454, 1055 cm^{-1}. Anal. Calcd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93; N, 6.00. Found: C, 77.32; H, 10.11; N, 5.77.

3-(3,5-Dimethyladamantan-1-yl)-2-oxopropionitrile (4f): ^{1}H NMR ($CDCl_3$, 270 MHz) δ 2.14 (s, 2H), 1.11–2.09 (m, 13H), 0.82 (s, 6H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 178.1, 120.8, 50.9, 48.5, 48.0, 42.9, 40.8, 34.2, 31.3, 30.5, 29.6; IR (NaCl) 2898, 2845, 1703, 1453 cm^{-1}. Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.68; H, 9.12; N, 5.97.

2-(3,5-Dimethyladamantan-1-yl)-3-hydroxysuccinonitrile (3g): identified as a mixture of diasteroisomers; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 3.51 (dd, J = 10.3, 11.4 Hz, 1H), 3.48 (dd, J = 6.8, 14.2 Hz, 1H), 1.17–2.19 (m, 19H), 0.88 (s, 6.67H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 112.0, 111.8, 110.8, 109.2, 65.9, 65.6, 50.3, 50.1, 46.9, 46.7, 42.6, 42.5, 39.0, 38.9, 33.3, 33.2, 31.3, 31.2, 30.1, 29.9, 29.0, 28.8, 15.2, 15.0; IR (NaCl) 3441, 2896, 2861, 1454, 1055 cm^{-1}. Anal. Calcd for $C_{16}H_{22}N_2O$: C, 74.38; H, 8.58; N, 10.84. Found: C, 74.35; H, 8.29; N, 10.85.

3-(3,5-Dimethyladamantan-1-yl)-2-hydroxypropionamide (3h): ^{1}H NMR ($CDCl_3$, 270 MHz) δ 6.26 (s, 1H), 5.67 (s, 1H), 4.11 (dd, J = 1.98, 9.57 Hz, 1H), 1.06–2.67 (m, 15H), 0.81 (s, 6H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 182.0, 69.9, 52.3, 49.6, 48.1, 44.4, 42.4, 35.1, 32.2, 31.3, 30.2; IR (NaCl) 3480, 2895, 1720, 1200 cm^{-1}. Anal. Calcd for $C_{15}H_{25}NO_2$: C, 71.67; H, 10.02; N, 5.57. Found: C, 71.81; H, 9.89; N, 5.41.

3-(3,5-Dimethyladamantan-1-yl)-2-oxopropionamide (4h): ^{1}H NMR ($CDCl_3$, 270 MHz) δ 6.80 (s, 1H), 5.48 (s, 1H), 2.71 (s, 2H), 1.06–2.06 (m, 13H), 0.84 (s, 6H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 199.2, 172.5, 51.1, 48.9, 47.6, 43.2, 41.2, 36.1, 31.6, 30.8, 29.9; IR (NaCl) 3421, 3189, 2895, 2840, 1684 cm^{-1}. Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 71.99; H, 9.28; N, 5.41.

***N*-(2-Hydroxy-2-methylpropionic acid methyl ester)-phthalimide (5):** ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.74–7.85 (m, 5H), 4.62 (s, 1H), 4.12 (s, 2H), 3.81 (s, 3H), 1.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 174.2, 163.3, 134.7, 128.7, 123.7, 83.5, 74.0, 52.9, 22.0; IR (NaCl) 3498, 2954, 1789, 1467, 1187 cm^{-1}. Anal. Calcd for $C_{13}H_{13}NO_5$: C, 55.91; H, 4.69; N, 5.02. Found: C, 55.82; H, 4.98; N, 4.74.

2-Adamantan-1-yl-3-hydroxysuccinic acid dimethyl ester (3i): identified as a mixture of diasteroisomers; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 4.59 (dd, J = 5.9, 7.3 Hz, 0.25H), 4.52 (dd, J = 2.3, 10.1 Hz, 1H), 3.87 (d, J = 10.1 Hz, 1H), 3.77 (s, 0.67H), 3.75 (s, 3H), 3.70 (s, 3H), 3.68 (s, 0.67H), 3.08 (d, J = 5.2 Hz, 0.25H), 2.48–2.52 (m, 1.25 Hz, 1.25H), 1.64–2.01 (m, 20H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 174.4, 174.3, 173.2, 172.7, 70.5, 69.1, 59.8, 57.8, 52.7, 52.4, 51.5, 51.3, 40.6, 40.4, 36.7, 36.6, 35.7, 35.3, 28.7, 28.6; IR (NaCl) 3500, 2904, 1735, 1435, 1236 cm^{-1}. Anal. Calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 64.66; H, 7.95.

2-Adamantan-1-yl-3-oxosuccinic acid dimethyl ester (4i): ^{1}H NMR ($CDCl_3$, 270 MHz) δ 4.04 (s, 1H), 3.87 (s, 3H), 3.70 (s, 3H), 1.68–1.99 (m, 15H); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 188.3, 167.4, 161.2, 62.8, 53.3, 52.1, 39.9, 37.6, 36.7, 28.5; IR (NaCl) 2906, 1735, 1435, 1236, 1157 cm^{-1}. Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.58; H, 7.60.

2-Hydroxy-3-(1-methylcyclohexyl)succinic acid dimethyl ester (3j): identified as a mixture of diasteroisomers; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 4.56 (dd, J = 5.8, 7.3 Hz, 0.25H), 4.49 (dd, J = 2.2, 9.9 Hz, 1H), 3.78 (d, J = 7.3 Hz, 1H), 3.77

(s, 3H), 3.76 (s, 0.67H), 3.69 (s, 3H), 3.68 (s, 0.67H), 2.85 (d, J = 2.2 Hz, 1H), 1.18 (s, 3H), 0.87–1.63 (m, 13H); ^{13}C NMR (CDCl$_3$, 270 MHz) δ 174.4, 174.1, 173.2, 172.7, 70.5, 69.5, 55.6, 55.4, 52.7, 52.5, 51.6, 51.5, 37.2, 37.0, 36.4, 36.2, 36.0, 35.9, 26.0, 25.9, 22.4, 22.2, 22.0, 21.8, 21.7, 21.6; IR (NaCl) 3498, 2927, 1746, 1434, 1255 cm^{-1}. Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found: C, 60.21; H, 8.43.

2-(1-Methylcyclohexyl)-3-oxosuccinic acid dimethyl ester (4j): ^{1}H NMR (CDCl$_3$, 270 MHz) δ 4.30 (s, 1H), 3.87 (s, 3H), 3.70 (s, 3H), 1.31–1.56 (m, 13H), 1.16 (s, 3H); ^{13}C NMR (CDCl$_3$, 270 MHz) δ 188.5, 168.0, 161.3, 61.0, 53.3, 52.1, 37.9, 36.6, 35.9, 25.8, 22.2, 21.5, 20.9; IR (NaCl) 2932, 1731, 1436, 1264, 1063 cm^{-1}. Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.79; H, 7.83.

2-Cyclohexyl-3-hydroxysuccinic acid dimethyl ester (3k): identified as a mixture of diastereoisomers; ^{1}H NMR (CDCl$_3$, 270 MHz) δ 4.41 (s, 1H), 3.78 (s, 0.67H), 3.77 (s, 3H), 3.70 (s, 0.67H), 3.68 (s, 3H), 3.45 (d, J = 3.3 Hz, 1H), 2.61 (dd, J = 3.3, 9.2 Hz, 1H), 2.71 (dd, J = 6.2, 6.9 Hz, 1H), 1.03–1.98 (m, 16.2H); ^{13}C NMR (CDCl$_3$, 270 MHz) δ 174.4, 174.1, 173.8, 173.6, 70.5, 69.3, 54.8, 54.2, 52.7, 52.4, 52.0, 51.8, 36.6, 36.4, 31.6, 31.5, 30.4, 30.2, 26.3, 26.2, 26.1, 26.0, 25.9; IR (NaCl) 3500, 2930, 1746, 1434, 1166 cm^{-1}. Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 58.70; H, 8.03.

2-Cyclohexyl-3-oxosuccinic acid dimethyl ester (4k): ^{1}H NMR (CDCl$_3$, 270 MHz) δ 3.92 (d, J = 7.3 Hz, 1H), 3.77 (s, 3H), 3.68 (s, 3H), 1.01–2.45 (m, 11H); ^{13}C NMR (CDCl$_3$, 270 MHz) δ 188.5, 168.5, 161.0, 60.0, 53.3, 52.3, 37.3, 31.0, 30.4, 26.1, 26.0, 25.9; IR (NaCl) 2929, 1731, 1436, 1264, 1054 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found: C, 59.36; H, 7.51.

2-Cyclooctyl-3-hydroxysuccinic acid dimethyl ester (3l): identified as a mixture of diastereoisomers: ^{1}H NMR (CDCl$_3$, 270 MHz) δ 4.51 (dd, J = 6.4, 7.0 Hz, 0.25H), 4.41 (dd, J = 3.3, 9.5 Hz, 1H), 3.83 (s, 3H), 3.78 (s, 0.67H), 3.77 (s, 3H), 3.70 (s, 0.67H), 3.36 (d, J = 9.5 Hz, 1H), 2.70 (dd, J = 3.3, 9.5 Hz, 1H), 1.33–2.24 (m, 19H); ^{13}C NMR (CDCl$_3$, 270 MHz) δ 174.4, 174.3, 173.8, 173.6, 70.4, 69.7, 54.6, 54.4, 52.7, 52.5, 52.0, 51.8, 35.9, 35.7, 30.3, 30.2, 29.1, 29.0, 27.2, 27.1, 27.0, 26.9, 26.4, 26.2, 25.7, 25.5, 25.0, 24.9; IR (NaCl) 3500, 2945, 1743, 1447, 1162 cm^{-1}. Anal. Calcd for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88. Found: C, 61.41; H, 8.83.

2-Cyclooctyl-3-oxo-succinic acid dimethyl ester (4l): ^{1}H NMR (CDCl$_3$, 270 MHz) δ 3.92 (d, J = 7.3 Hz, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 3.43 (s, 1H), 1.31–2.36 (m, 15H); ^{13}C NMR (CDCl$_3$, 270 MHz) δ 190.2, 168.5, 168.1, 54.2, 52.1, 51.9, 35.7, 30.2, 29.1, 27.2, 27.0, 26.3, 25.4, 24.9; IR (NaCl) 2898, 1735, 1452, 1270, 1161 cm^{-1}. Anal. Calcd for $C_{14}H_{22}O_5$: C, 62.20; H, 8.20. Found: C, 61.95; H, 8.01.

3-Hydroxy-2-oxo-1-oxaspiro[4.5]decane-4-carboxylic acid methyl ester (6k): ^{1}H NMR (CDCl$_3$, 270 MHz) δ 5.01 (dd, J = 4.0, 10.6 Hz, 1H), 3.82 (s, 3H), 3.66 (d, J = 4.0, 1H), 3.10 (d, J = 10.6 Hz, 1H), 1.19–1.98 (m, 11H); ^{13}C NMR (CDCl$_3$, 270 MHz) δ 174.8, 169.2, 88.1, 69.6, 58.5, 52.7, 37.2, 33.1, 24.6, 22.0, 21.8; IR (NaCl) 3479, 2950, 1778, 1434, 1237, 947 cm^{-1}. Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.88; H, 7.07. Found: C, 57.76; H, 6.89.

3-Hydroxy-2-oxo-1-oxaspiro[4.7]dodecane-4-carboxylic acid methyl ester (6l): ^{1}H NMR (CDCl$_3$, 270 MHz) δ 5.00 (dd, J = 2.2, 10.6 Hz, 1H), 3.81 (s, 3H), 3.48 (dd, J = 2.2, 7.0 Hz, 1H), 3.12 (d, J = 10.6 Hz, 1H), 1.21–2.18 (m, 15H); ^{13}C NMR (CDCl$_3$, 270 MHz) δ 174.7, 169.5, 86.9, 70.3, 58.8, 52.6, 37.9, 32.0, 27.9, 27.0, 24.2, 21.7, 21.2; IR (NaCl) 3448, 2925, 1789, 1440, 1255 cm^{-1}. Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.82; H, 7.97.

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Supporting Information Available: Copies of ^{13}C and ^{1}H NMR and IR spectra for all of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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